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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,342	11/20/2003	Francisco J. Cifuentes	10030679-1	1237

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EXAMINER
AGRAWAL, RITESH

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,342	CIFUENTES ET AL.	
	Examiner	Art Unit	
	Ritesh Agrawal	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *12-19,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 20-26* is/are rejected.

7)☒ Claim(s) *5 and 21-26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Amendments

1. Applicant's election of Group I (claims 1-11 and 20-26) in the reply filed on 10/30/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 12-19 and 27-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Information Disclosure Statement

2. The Information Disclosure Statement filed 03/12/04 has been entered and considered. Initialed copies of the form PTO-1449 are enclosed with this action.

Specification

3. The disclosure is objected to because of the following:

The use of the trademarks CY3, CY5, TEXAS RED, and ZOOSEQ have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. CY3 and CY5 can be found, for example, on page 11 of the specification. TEXAS RED can be found on page 12 of the specification, and ZOOSEQ can be found on page 45 of the specification.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The title is specifically drawn to a method for evaluating tissue pairs but the claims are drawn to various methods related to sample pair selection, probe design, array production, data forwarding, and analyte detection.

The abstract of the disclosure is objected to because it is specifically drawn to selecting nucleic acid sample pairs whereas the invention as a whole, encompasses several other methods. Correction is required. See MPEP § 608.01(b).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11 and 20-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation in step (b) of "genes that exhibit differential expression." The measurement of "differential expression" requires the comparison of expression levels between different samples. It is unclear what samples are being

compared to obtain a measurement of "differential expression." While "sample pairs" is recited in step (a) it's unclear as to whether the differential expression is between two samples of a pair or between different pairs.

Claim 1 recites the limitation "said genes" in line 10. There are multiple uses of the term genes including those that are represented by the probes, the expected genes in the sample, and those that are part of the maximized number of genes. It is unclear as to which of these genes the phrase refers.

Claim 2 recites the limitation "each gene in step (a)" in lines 1-2. Step (a) recites genes that are represented by probes and expected genes in a sample. It is unclear as to which of these genes the phrase refers. Furthermore, if the phrase refers to each gene in the sample, it is unclear as to how to make a determination of differential expression given that only some genes in the sample are represented by probes.

Claim 2 recites the limitation "probes for each gene" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. There is no prior reference to multiple probes representing a gene, only "probes representing a set of genes" as in lines 5-6 of claim 1.

Claim 9 recites the limitation in step (b) of "said gene exhibits or does not exhibit differential expression." The measurement of "differential expression" requires the comparison of expression levels between different samples. It is unclear what samples are being compared to obtain a measurement of "differential expression." While "sample pairs" is recited in step (b) it's unclear as to whether the differential expression is between two samples of a pair or between different pairs.

Claim 9 recites the limitation "each combination of said nucleic acid sample pairs to be evaluated" in lines 13-14. There is insufficient antecedent basis for this limitation in the claim. There is no prior reference to a "combination of said nucleic acid sample pairs" in any of the previous method steps.

Claim 9 recites the limitation "data from step (c)" in line 13. There is insufficient antecedent basis for this limitation in the claim. There is no reference to the term "data" in step (c) of claim 9. It is therefore unclear as to what information from step (c) is being tabulated.

Claim 21 recites the limitation "said candidate nucleic acid probe sequences" in line 8. There is insufficient antecedent basis for this limitation in the claim. There is no prior reference to "candidate nucleic acid probe sequences" only "candidate probe sequences."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-4, and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonaventure et al. (Brain Research, Vol. 943, Pages 38-47, July, 2002).

The claims are drawn to a method of selecting a combination of nucleic acid sample pairs comprising:

(a) conducting differential expression experiments using nucleic acid sample pairs and nucleic acid probes immobilized on a substrate

(b) selecting a nucleic acid sample pair by maximizing the number of differentially expressed genes

Bonaventure et al. disclose carrying out differential expression experiments where they look for genes enriched in various brain nuclei using cDNA microarrays (abstract). From these experiments, they select locus coeruleus (LC) for discussion in the paper where these nuclei have the maximum number of enriched (or differentially expressed) genes (page 42, 1st column, 3rd paragraph, lines 9-10).

With respect to claim 2, Bonaventure et al. disclose using intensities for each gene (page 40, 1st column, 2nd paragraph, lines 11-14) and calculating a median value across probes (page 40, 1st column, 2nd paragraph, line 16) and determining the statistical significance of the spread in values (page 40, 1st column, 2nd paragraph, lines 16-20) thereby determining whether they probe values cluster.

With respect to claims 3 and 4, Bonaventure et al. disclose using the raw signal intensities to produce log-treated values (page 40, 1st column, 2nd paragraph, line 20).

With respect to claim 6, Bonaventure et al. carry out a plurality of differential gene expression experiments using a plurality of experimental sets in using a plurality of cellular nuclei (see table 1).

With respect to claims 7-8, Bonaventure et al. disclose that each sample is hybridized to a separate substrate (page 40, 1st paragraph, line 3), as in claim 8, and, in the process of being hybridized to separate substrates they are being hybridized to a substrate, as in claim 7.

6. Claims 1-8 and 20-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Collins et al. (US Publication # 2004/0101846, filed November 22nd, 2002).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a method of selecting a combination of nucleic acid sample pairs comprising:

(a) conducting differential expression experiments using nucleic acid sample pairs and nucleic acid probes immobilized on a substrate

(b) selecting a nucleic acid sample pair by maximizing the number of differentially expressed genes

Collins discloses selection of nucleic acid sample pairs by hybridizing nucleic acid sample pairs to nucleic acids on microarrays and selecting for those sample pairs that maximize the number of mRNAs that are differentially expressed (paragraph 70, lines 1-8).

With respect to claim 2, Collins discloses evaluating each probe (representative of genes) and clustering based upon evaluation of differential expression (see, for example, paragraphs 51,52).

With respect to claims 3-4, Collins discloses consideration of the parameter of LogRatio in determining differential expression (for example, paragraph 71).

With respect to claim 5, Collins discloses that the parameters include probability of significant difference and number of probes of significant difference (paragraph 99, lines 8-10).

With respect to claim 6, Collins discloses that the sample pairs are tissue pairs (paragraph 70, lines 6-8).

With respect to claims 7-8, Collins discloses contacting sample pairs with either a single substrate or separate substrates (paragraph 69).

With respect to claim 20, Collins discloses evaluating candidate probes using sample pairs identified through the method of claim 1 (see paragraph 69).

With respect to claim 21, Collins discloses the method (claim 1) where Collins has previously defined that the evaluation employs a nucleic acid sample pair selected by the method of claim 1 (as cited for claim 20).

With respect to claim 22, Collins discloses the method (see, for example, claims 18 or 19).

With respect to claim 23, Collins disclose the method (see, for example, paragraph 116).

With respect to claim 24, Collins disclose the method (see, for example, paragraph 116, lines 30-33).

With respect to claim 25, Collins disclose the method (see, for example, paragraph 115).

With respect to claim 26, Collins disclose the method (see, for example, paragraph 116, lines 32-33).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 20-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventure et al. (Brain Research, Vol. 943, Pages 38-47, July, 2002) as applied to claims 1-4, and 6-8 above, and further in view of Dooley et al. (US Patent Publication # 2001/0046671, Publication Date Nov. 29, 2001).

The claims are drawn to a method of identifying a sequence of nucleic acid suitable for use as a substrate immobilized probe comprising:

(a) identifying a plurality of candidate probes

(b) empirically evaluating each of the candidate probes using the sample pair of Claim 1

(c) clustering candidate probes into groups

(d) selecting one of the groups

(e) choosing a candidate probe from the selected group

Dooley et al. disclose identifying a plurality of candidate probes that are chosen for their expression in a given sample type (paragraph 12, lines 11-14). They empirically

evaluate these probes against a specified sample for which they are specifically designing the probes (Fig. 1, II, 3). They disclose clustering of probe sequences (Fig. 1, III, 4), selecting those that are relevant to the desired application (Fig. 1, IV, 1) and then specifically choosing examples that are appropriate (fig. 1, IV, 2-4).

However, Dooley et al. do not disclose using a sample pair from claim 1.

Bonaventure et al. disclose obtaining a sample pair of claim 1.

It would have been obvious, for one of ordinary skill in the art, at the time the invention was made, to modify the method of Bonaventure et al. to use it in combination with the method of Dooley et al. to prepare probes that are specific for the tissue pair of Bonaventure et al. One of ordinary skill in the art would have been motivated to do this because, as suggested by Dooley et al., by designing an "informative array", Bonaventure et al. would be more likely do identify differentially expressed genes (paragraph 19, lines 4-8).

With respect to claim 22, the combination of Dooley et al. disclose the method of claim 21 for identifying nucleic acid probes (as cited above), and Dooley et al. disclose synthesizing and depositing said probes in an array on a substrate (for example, fig. 1, IV, 4).

With respect to claim 23, Dooley et al. disclose contacting the produced array with a sample and detecting the presence of complexes (for example, fig. 1, V, first bullet, and references therefrom).

With respect to claims 24 and 26, Dooley et al. disclose forwarding data from a detector where the data in then received by a computer (paragraph 8, lines 14-17).

With respect to claim 20, claim 21 represents a species of claim 20 and thus since the combination of Dooley et al. and Bonaventure et al. disclose the method of claim 21, they anticipate the method of claim 20.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 20-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 and 18-19 of copending application 10/303160. (***The vogel type, i.e. genus makes species obvious if species are specifically disclosed in that copending application)***

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably

distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claim 21 of the instant application is drawn to a method for identifying a sequence of a nucleic acid that is suitable for use as a substrate immobilized probe comprising (a) identifying a plurality of candidate probe sequences, (b) empirically evaluating each of said candidate probe sequences wherein the empirical evaluation employs a nucleic acid sample pair chosen by the method of claim 1, (c) clustering said candidate probe sequences, (d) selecting one of said one or more groups of clustered sequences, and (e) choosing a candidate probe sequence from said selected group.

While the exact wording of claim 1 of the '160 application is not the same as that of claim 21 of the instant application, the only difference in scope is in step b with the only difference being the additional requirement of the empirical evaluation employing a nucleic acid sample pair as selected by of claim 1 in the instant application versus just an empirical evaluation in claim 1 of the '160 application. Thus the "empirical evaluation" step of claim 1 of the '160 application is generic to the "empirical evaluation employ[ing] a nucleic acid sample pair selected by a method according to Claim 1" step of the instant claim 21.

The portion of the specification of the '160 application that supports the recited "empirical evaluation" procedure includes an embodiment that would anticipate the "empirical evaluation employ[ing] a nucleic acid sample pair" step of the instant claim 21. Paragraph 70, lines 6-10 of the '160 application specifically disclose an empirical evaluation wherein the empirical evaluation employs a nucleic acid sample pair selected by a method of instant claim 1. Claim 21 of the instant application cannot be considered patentably distinct over claim 1 of the '160 application when there is a specifically disclosed embodiment in the prior application specification that supports claim 1 of that application and falls within the scope of the instant claim 21 because it would have been obvious to one having ordinary skill in the art to modify the empirical evaluation step of claim 1 of the '160 application by selecting a specifically disclosed embodiment that supports the claim, i.e. the "empirical evaluation" step disclosed in that application.

With respect to claim 20, claim 21 represents a species of claim 20, and it is therefore also obvious in light of the prior application.

With respect to claim 22 it is drawn to a method of preparing a nucleic acid array based upon identifying nucleic acid probes using the method of claim 21, and claims 18-19 of the prior application disclose a method of preparing an array of nucleic acids based upon identifying nucleic acid probes as in claim 1 of the prior application

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 20-22 are directed to an invention not patentably distinct from claims 1 and 18-19 of commonly assigned application 10/303160. Specifically, the claims are not patentably distinct as addressed above.

10. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned application 10/303160, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim Objections

11. Claim 5 is objected to because of the following informalities: The claim recites two different parameters to be considered yet both parameters are labeled as parameter (i). Appropriate correction is required.

Claims 21-26 are objected to because of the following informalities: Claim 21 recites the phrase "to as said sequence of said nucleic acid" in step (e), lines 1-2. This phrase does not make grammatical sense. Appropriate correction is required.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ritesh Agrawal whose telephone number is (571) 272-2906. The examiner can normally be reached on 8:30 AM - 5:00 PM M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ritesh Agrawal

SHUBO (JOE) ZHOU, PH.D.
PATENT EXAMINER